REMARKS/ARGUMENTS

Entry of the foregoing and favorable reconsideration and reexamination of the subject application, as amended, and in light of the remarks that follow, are respectfully requested.

The Examiner's correction of previously misnumbered claims 45 and 46 is appreciated; claim numbering in the present amendment corresponds to the Examiner's correction. It is noted that, as a result of the present amendment, the misnumbered claims have been canceled.

By the present amendment, claims 36, 37, 40, 55, 56 and 57 have been canceled without prejudice or disclaimer of the subject matter contained therein. Claims 10, 27, 28, 38, 44, 50 and 53 have been further amended to further clarify the present invention. Support for the concentration of nicotine or nicotine derivative and L-DOPA appear at least on page 4, first paragraph of the specification. Applicants submit that no new matter has been added via this claim amendment.

Claims 41 and 45 have been rejected under 35 U.S.C. §112, first paragraph. In rendering this rejection, the Examiner states that there is no support in the specification for 3 mg/kg/day in claim 41 and no support for 160 mg per day for claim 45. Applicants respectively traverse this rejection.

Specific support for the recited ranges can be found at of the specification, wherein it is stated with regard to L-DOPA:

> "A preferred dose is in the range 0.2 to 3 mg per kilogram per 24 hours."

(page 4, lines 8-9)

Furthermore, with regard to nicotine, the specification states:

> "This treatment must not be interrupted and the doses must be constantly maintained at between 93 mg and 160 mg per day."

(page 11, lines 3-5) Therefore, Applicants submit that there is indeed support in the specification for claims 41 and 45. Withdrawal of this rejection is therefore respectfully requested.

Claims 10, 12 to 14, 18 to 19, 21 to 28, 31 to 41, 44 to 46 and 49 to 57 have been rejected under 35 U.S.C. § 112, first paragraph as lacking enablement "for any and all doses of nicotine or L-DOPA." Additionally, the Examiner states, "Page 4, lines 1-8, discloses the nature of the instant invention." It is noted that this portion of the specification refers to a dosage range of nicotine or a nicotine derivative.

It is respectfully suggested that the teachings embodied in the present application, including the detailed disclosure and examples, provide a sufficient basis for one skilled in the art to use the invention in the scope as originally claimed, and the Examiner has not offered a basis in support of a contrary view. However, solely to expedite the prosecution of this application and not to acquiesce to the rejection, the independent claims have been amended to recite the concentration of nicotine or nicotine derivative. Therefore, it is respectfully requested that this rejection be withdrawn in view of the amendment.

Claims 10, 12 to 14, 44 to 46, 50 to 55, 56 and 57 have been rejected under 35 U.S.C. §112, second paragraph. In support of the rejection the Examiner argues that the term "progressive" is indefinite in the claims. The claims have been amended to delete the term progressive and to describe the drug administration as "doses which increase over three consecutive months followed by stabilized doses after three months." Support for this amendment can be found, for example, on page 4,

lines 26 to 30 of the specification as filed. Therefore, in view of this amendment, withdrawal of this aspect of the rejection is respectfully requested.

Claims 10, 12 to 15, 18 to 19, 21 to 28, 31 to 41, 44 to 46 and 49 to 57 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Domino et al.* For the following reasons, this rejection is respectfully traversed.

To briefly review, the present invention relates to a drug composition for administration to a subject orally, subcutaneously, transdermally or any combination thereof, comprising as a first component nicotine or a nicotine derivative, wherein said nicotine or nicotine derivative is present in an amount sufficient to be administered to said subject at a rate of from 0.2 mg to 5 mg per day per kilogram of body weight of said subject, and a second component comprising L-DOPA in a dose at least 30% lower than the effective dose when L-DOPA is administered in the absence of said first component. This drug composition can be used to treat neurological disorders and more specifically, Parkinson's Disease and Tourette's Syndrome.

Furthermore, it was known in the art, especially for the treatment of Parkinson's Disease, that L-DOPA, when administered alone at dosages of about 12.5 mg/kg, was effective to treat some of the symptoms of this disease. However, it was not known, nor could it be expected by those skilled in this art, that treatment with nicotine and lower doses of L-DOPA; i.e., at least 30% lower than the dose normally given alone, was more efficient for the treatment of neurological disorders and especially Parkinson's Disease. This phenomenon is contrary to accepted practice since the skilled artisan would expect that a lower dosage of a drug would result in a less effective treatment of the disease. Therefore, Applicants submit that

this is evidence of an unexpected result and is particularly relevant with respect to the rejection in view of the cited prior art.

Turning now to the rejection, a detailed analysis of the reference relied on by the Examiner, *Domino et al.*, shows that it fails to teach or suggest the use of a drug composition that has nicotine or a nicotine derivative in a concentration of 0.2 mg to 5 mg per day per kilogram of body weight and wherein the L-DOPA is in a dose at least 30% lower than the effective dose when L-DOPA is administered in the absence of nicotine or the nicotine derivative. In fact, *Domino et al.* disclose using 0.1 mg/kg and 0.320 mg/kg nicotine in combination with 12.5 mg/kg of L-DOPA. As can be seen from *Domino et al.* at page 415, column 2, last paragraph, the dose of 12.5 mg/kg of L-DOPA was chosen since it was the dose previously shown to be an effective dose when given alone; i.e., without nicotine.

In contrast, in the present invention it is taught to administer 30% less of L-DOPA when used in combination with the appropriate amount of nicotine or a nicotine derivative. To reiterate, there is no teaching or suggestion in *Domino et al.* that the amount of L-DOPA can be decreased while maintaining the efficacy of a combination drug composition with nicotine.

Furthermore, with respect to Claims 15, 28 and 53, *Domino et al.* does not suggest the further combination of nicotine or a nicotine derivative with L-DOPA and a dopaminergic agonist as set forth in these claims. Rather, *Domino et al.* teach using nicotine and the full dopamine D2 receptor agonist N-0923, but not L-DOPA. Moreover, no effect was seen using the combination of the agonist N-0923 and nicotine with respect to any effect on the monkey test subjects. Thus, these results would lead the skilled artisan away from using the combination in the reference and no other combination is suggested.

It is respectfully emphasized that in order to establish a *prima facie* case of obviousness, "(t)he prior art reference (or references when combined) must teach or suggest all the claim limitations." (MPEP § 2142) Furthermore, there is a precaution to be observed when a single reference is relied on for such a rejection. As stated by the Federal Circuit in *Sibia Neurosciences Inc. v. Cadus Pharmaceutical Co.*:

> "In appropriate circumstances, a single prior art reference can render a claim obvious. *See, e.g. B.F. Goodrich Co. v. Aircraft Braking Sys. Corp.*, 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996); *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). However, there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion."

(55 USPQ2d 1927, 1931, Fed. Cir. 2000)

In the present rejection there is a total absence of any showing of such a suggestion or motivation to support departing from the limited teaching of *Domino et al.* Therefore, since *Domino et al.* fail to teach or even suggest to a skilled artisan to use a significantly lower dosage of L-DOPA, or to combine nicotine, L-DOPA and a dopaminergic agonist, Applicants submit that the presently claimed invention is not obvious in view of *Domino et al.*

Thus, in view of the above, withdrawal of this rejection is respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested

that she telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,

By _____
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